General

Guideline Title

Management of acute and recurrent gout: a clinical practice guideline from the American College of Physicians.

Bibliographic Source(s)

Qaseem A, Harris RP, Forciea MA, Clinical Guidelines Committee of the American College of Physicians. Management of acute and recurrent gout: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017 Jan 3;166(1):58-68. [94 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the overall quality of evidence (high, moderate, low, or insufficient) and the strength of the recommendations (strong, weak) are provided at the end of the "Major Recommendations" field.

Recommendation 1: The American College of Physicians (ACP) recommends that clinicians choose corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine to treat patients with acute gout. (Grade: strong recommendation, high-quality evidence)

High-quality evidence showed that corticosteroids, NSAIDs, and colchicine are effective treatments to reduce pain in patients with acute gout. Gout symptoms are mostly caused by inflammatory reaction to the deposition of urate crystals, which results from an increase in serum urate level above its saturation point in the blood. Hence, most medications that are used to target anti-inflammatory responses help to reduce the symptoms. Contraindications, harms, and costs vary among treatments.

Corticosteroids should be considered as first-line therapy in patients without contraindications because they are generally safer and a low-cost treatment option. Steroids are among the most effective anti-inflammatory medications available and have been shown to be as effective as NSAIDs for managing gout, with fewer adverse effects. Prednisolone at a dose of 35 mg for 5 days has been successfully used to treat acute gout. Adverse effects associated with long-term use of corticosteroids include dysphoria, mood disorders, elevation of blood glucose levels, immune suppression, and fluid retention.

Corticosteroids are contraindicated in patients with systemic fungal infections or known contraindications.

Moderate-quality evidence showed no difference between different types of NSAIDs, including indomethacin. Adverse effects associated with NSAIDs include dyspepsia and potential gastrointestinal perforations, ulcers, and bleeding. Patients in whom NSAIDs may be contraindicated include those with renal disease, heart failure, or cirrhosis. Although indomethacin is commonly considered as the first-line NSAID for treatment of acute gout, there is no evidence that it is more efficacious than other NSAIDs, such as naproxen and ibuprofen.

A generic formulation of colchicine is now available for gout treatment, but it is still more expensive than NSAIDs or corticosteroids. Adverse effects associated with colchicine include gastrointestinal issues (such as diarrhea, nausea, vomiting, cramps, and pain) and, infrequently, headache and fatigue. Colchicine is contraindicated in patients with renal or hepatic impairment who are using potent cytochrome P450 3A4 inhibitors or P-glycoprotein inhibitors.

Recommendation 2: ACP recommends that clinicians use low-dose colchicine when using colchicine to treat acute gout. (Grade: strong recommendation, moderate-quality evidence)

Moderate-quality evidence suggests that lower doses of colchicine (1.2 mg followed by 0.6 mg 1 hour later) are as effective as higher doses (1.2 mg followed by 0.6 mg/h for 6 hours) at reducing pain and are associated with fewer gastrointestinal adverse effects.

Recommendation 3: ACP recommends against initiating long-term urate-lowering therapy in most patients after a first gout attack or in patients with infrequent attacks. (Grade: strong recommendation, moderate-quality evidence)

Although evidence supports the benefits of using urate-lowering therapy for shorter durations to reduce gout flares, the benefits of long-term use (≥12 months) in patients with a single or infrequent gout attacks (<2 per year) have not been studied. Urate-lowering therapy is not necessary in cases where the patient would have no or infrequent recurrences. In cases of recurrent gout (≥2 episodes per year) or problematic gout (for example, gout associated with tophi, chronic renal disease, or urolithiasis), shared decision making with the patient is warranted to review possible harms and benefits of urate-lowering therapy.

Recommendation 4: ACP recommends that clinicians discuss benefits, harms, costs, and individual preferences with patients before initiating urate-lowering therapy, including concomitant prophylaxis, in patients with recurrent gout attacks. (Grade: strong recommendation, moderate-quality evidence)

After resolution of acute gout, some patients may have recurrent episodes. Some patients have no or few attacks over many years, whereas others have more frequent attacks. Although evidence is inadequate to predict which patients will have more problems, those with higher serum urate levels (especially >476 µmol/L [>8 mg/dL]) are at greater risk. Some may prefer to initiate long-term therapy to prevent future gout attacks, whereas others may prefer to treat flares if they occur. Patients who decide not to initiate urate-lowering therapy can revisit their decision if they have multiple recurrences of acute gout.

Febuxostat (40 mg/d) and allopurinol (300 mg/d) are equally effective at decreasing serum urate levels. However, these drugs are associated with adverse effects, including rash with allopurinol and abdominal pain, diarrhea, and musculoskeletal pain with febuxostat.

Data on the most appropriate duration of urate-lowering therapy are insufficient. Moderate- to high-quality evidence suggests that urate-lowering therapy reduces the risk for acute gout attacks after 1 year, but not within the first 6 months of treatment.

High-quality evidence showed that prophylactic therapy with low-dose colchicine or low-dose NSAIDs reduces the risk for acute gout attacks in patients initiating urate-lowering therapy. Moderate-quality evidence also showed that continuing prophylactic treatment for more than 8 weeks was more effective than shorter durations to help prevent gout flares in patients initiating urate-lowering therapy.

Definitions

Grading Strength of Evidence

High: The reviewers are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. The reviewers believe that the findings are stable, i.e., another study would not change the conclusions.

Moderate: The reviewers are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. The reviewers believe that the findings are likely to be stable, but some doubt remains.

Low: The reviewers have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). The reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.

Insufficient: The reviewers have no evidence, they are unable to estimate an effect, or they have no in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Acute or recurrent gout

Guideline Category

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Rheumatology

Intended Users

Advanced Practice Nurses

Health Care Providers

Physician Assistants

Physicians

Guideline Objective(s)

To provide guidance on the management of acute and recurrent gout in adults

Target Population

Adults (≥18 years of age) with acute or recurrent gout

Interventions and Practices Considered

1. Nonsteroidal anti-inflammatory drugs (NSAIDS)
2. Corticosteroids
3. Colchicine (low-dose versus high-dose)
4. Long-term urate-lowering therapy (not recommended)
5. Discussion of benefits, harms, costs, patient preferences before initiating urate-lowering therapy for recurrent gout

Note: The following interventions/practices were considered but there was inconclusive evidence to make recommendations: treat-to-target strategy versus a treat-to-avoid-symptoms strategy in patients receiving urate-lowering therapy; effect of urate-lowering treatment on adverse health outcomes beyond acute gout; duration of urate-lowering treatment; treatment in different patient groups (e.g., patient demographic characteristics, comorbidities, gout severity, clinical presentation, or laboratory values); dietary treatments; long-term effects of febuxostat.

Major Outcomes Considered

- For acute gout treatment (Key Question [KQ]1)
  - Efficacy
    - Short-term health outcomes (days following acute flare)
      - Pain
      - Joint swelling, tenderness
    - Longer-term health outcomes
      - Serum uric acid
      - Pain
      - Joint swelling, tenderness
      - Activities of daily living (ADLs)
      - Patient global assessment
      - Recurrence
    - Safety
      - Gastrointestinal and renal side effects (nonsteroidal anti-inflammatory drugs [NSAIDS], colchicine)
      - Steroid-induced osteoporosis, diabetes

- For diet and other lifestyle therapy (KQ2)
  - Efficacy
    - Intermediate outcomes: serum and/or urine uric acid
    - Final health outcomes: recurrence and outcomes listed for pharmacologic treatments
  - Harms
- For chronic gout treatment (uric acid-lowering therapy), monitoring, and discontinuation (KQ3-5)
  - Efficacy
    - Intermediate outcomes: serum uric acid
    - Final health outcomes: pain, joint swelling, tenderness associated with the development of tophi, ADLs, patient global assessment, risk for comorbidities/mortality, recurrence of gout attacks (flares)
  - Safety
    - Inflammatory effects, including skin rash
    - Hematologic effects
    - Cardiovascular effects
    - Liver dysfunction
    - Renal dysfunction
- For anti-inflammatory prophylaxis with urate-lowering therapy (same outcomes as for acute gout therapy)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was conducted by the Agency for Healthcare Research and Quality's (AHRQ's) Southern California Evidence-based Practice Center–RAND Corporation (see the "Availability of Companion Documents" field).

Data Sources and Searches

The reviewers searched (without language restrictions) for systematic reviews and original research studies in PubMed, EMBASE, the Cochrane Collaboration, and the Web of Science, using the terms "gout" and "gouty" and terms for tophi. The start date of the searches was 1 January 2010, which was at least 1 year before the search dates for the most recent systematic reviews, and the end date was 1 March 2016. Relevant references were obtained from 29 recent systematic reviews. The reviewers searched ClinicalTrials.gov from inception to 1 March 2016 and the Web of Science from 1 January 2010 through 1 March 2016, and they contacted manufacturers of prescription medications used to treat gout for recently completed studies and unpublished or non–peer-reviewed study findings in July 2014. Appendix Table 1 of the systematic review provides detailed search methods (see the "Availability of Companion Documents" field).

Study Selection

Two reviewers independently screened records (titles, abstracts, and articles) to identify reviews and studies that reported on the benefits (randomized trials) or harms (observational studies and trials) of treatment and management strategies for gout. The reviewers examined only medications approved by the U.S. Food and Drug Administration (FDA), except for nonsteroidal anti-inflammatory drugs (NSAIDs), which are commonly used to treat gout. As suggested by the American College of Physicians (ACP)

Clinical Guidelines Committee, the reviewers excluded pegloticase and lesinurad, which primary care physicians are unlikely to prescribe. Studies that enrolled participants with no formal gout diagnosis (based on either synovial fluid analysis or a clinical diagnosis) were excluded.

Number of Source Documents

A total of 7928 titles/abstracts were identified for review (see the literature flow diagram in the systematic review [see the "Availability of Companion Documents" field]). A total of 155 articles met the inclusion criteria. Of these, 22 evaluated dietary therapy or traditional Chinese medicine; details about the inconclusive evidence from those studies are in the evidence report.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Grading Strength of Evidence

High: The reviewers are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. The reviewers believe that the findings are stable, i.e., another study would not change the conclusions.

Moderate: The reviewers are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. The reviewers believe that the findings are likely to be stable, but some doubt remains.

Low: The reviewers have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). The reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.

Insufficient: The reviewers have no evidence, they are unable to estimate an effect, or they have no in the estimate of effect for this outcome. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): A systematic evidence review was conducted by the Agency for Healthcare Research and Quality's (AHRQ's) Southern California Evidence-based Practice Center–RAND Corporation (see the "Availability of Companion Documents" field).

Data Extraction and Quality Assessment

Study-level details were abstracted by one reviewer and checked by a second reviewer, with reconciliation of disagreements by group discussion. Risk of bias of individual studies was assessed independently by 2 reviewers using an adapted Cochrane risk-of-bias tool, with reconciliation of disagreements by the project lead. A modified AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool was used to assess

the quality of systematic reviews.

Data Synthesis and Grading

The reviewers deemed studies to be too few in number and too heterogeneous to support new meta-analysis. They assessed the overall strength of evidence as high, moderate, low, or insufficient for each conclusion by using guidance suggested by the Effective Health Care Program. The reviewers also applied criteria proposed by Bradford Hill for causality when judging strength of evidence, including the strength, consistency, and specificity of the association; the temporal relationship; the "biologic gradient" or dose–response curve; the biologic plausibility; and coherence.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These recommendations are based on a background evidence paper and a systematic evidence review sponsored by the Agency for Healthcare Research and Quality (AHRQ) (see the "Availability of Companion Documents" field).

Key Questions (KQs)

The KQs that guided the review are based on questions posed by the American College of Physicians (ACP):

Key Question 1: Acute Gout Treatment

> In patients with acute gout, what are the benefits and harms of different pharmacologic therapies?
> Does effectiveness (benefits and harms) differ according to patient baseline demographic characteristics and comorbid conditions (including renal function)?
> Does effectiveness (benefits and harms) differ according to disease severity, including initial clinical presentation (e.g., extent of joint involvement and time since start of flare) and laboratory values (serum urate [UA] levels)?

Key Question 2: Dietary and Lifestyle Management of Gout

> In adults with gout, what are the benefits and harms of different dietary therapies and lifestyle measures on intermediate (serum UA levels) and final health outcomes (including recurrence of gout episodes and progression [e.g., development of tophi])?
> Does effectiveness and comparative effectiveness of dietary modification differ according to disease severity (including presence of tophi and baseline serum UA level), underlying mechanisms of hyperuricemia, or baseline demographic and comorbid characteristics?

Key Question 3: Pharmacologic Management of Hyperuricemia in Patients with Gout

> In adults with gout, what are the benefits and harms of different pharmacologic therapies on intermediate (serum UA levels) and long-term clinical health outcomes (including recurrence of gout episodes and progression)?
> Does effectiveness and comparative effectiveness of urate-lowering therapy differ according to disease severity (including presence of tophi and baseline serum UA), underlying mechanisms of hyperuricemia, or baseline demographic and comorbid characteristics?
> What is the effect of dietary modification in combination with pharmacologic therapy?

Key Question 4: Treatment Monitoring of Patients with Gout

> In adults with gout, does monitoring serum urate levels with pharmacologic treatment and/or dietary

and/or lifestyle change measures (e.g., adherence) improve treatment outcomes?
Is achieving lower subsequent serum urate levels (<297 vs. 297 to 416 µmol/L [<5 vs. 5 to 7 mg/dL]) associated with decreased risk for recurrent acute gout attack, progression to chronic arthritis or disability, resolution of tophi, or other clinical outcomes (including risk for comorbidities or progression of comorbidities) or patient-reported outcomes?

Key Question 5: Discontinuation of Pharmaceutical Management for Patients Receiving Acute or Chronic Gout Medications

In adults with gout, are there criteria that can identify patients who are candidates for discontinuing:

Urate-lowering therapy?
Anti-inflammatory prophylaxis against acute gout attack, for patients receiving urate-lowering therapy after an acute gout attack?

Grading the Evidence and Developing Recommendations

This guideline was developed by the American College of Physicians (ACP) Clinical Guidelines Committee (CGC) according to ACP's guideline development process, details of which may be found in the methods paper (see the "Availability of Companion Documents" field). The CGC used the evidence tables in the systematic review and AHRQ report (see the "Availability of Companion Documents" field) when reporting the evidence and graded the recommendations by using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

The American College of Physicians' Guideline Grading System*

Quality of Evidence	Strength of Recommendation	
	Benefits Clearly Outweigh Risks and Burden or Risks and Burden Clearly Outweigh Benefits	Benefits Finely Balanced With Risks and Burden
High	Strong	Weak
Moderate	Strong	Weak
Low	Strong	Weak
Insufficient evidence to determine net benefits or risks		

*Adopted from the classification developed by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) workgroup.

Cost Analysis

A cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The guideline went through a peer review process through the journal and was posted online for comments from American College of Physicians (ACP) Governors and Regents. All comments were read and carefully considered by the authors, and important issues were also discussed by the Clinical

Guidelines Committee (CGC).

This guideline was approved by the ACP Board of Regents on November 7, 2015.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Acute gout treatment (colchicine, nonsteroidal anti-inflammatory drugs [NSAIDs], corticosteroids, corticotropin): reduction of pain
- Prophylaxis during serum urate-lowering therapy (low-dose colchicine and low-dose NSAIDs): reduced acute gout flares

Potential Harms

- *Colchicine*: gastrointestinal adverse effects, such as diarrhea, nausea, cramps, and vomiting
- *Nonsteroidal anti-inflammatory drugs (NSAIDs)*: dyspepsia and potential gastrointestinal perforations, ulcers, and bleeding; long-term use of higher doses can cause chronic renal insufficiency
- *Corticosteroids*: mood disorders and dysphoria, elevation of blood glucose levels, immune suppression, and fluid retention
- *Corticotropin*: unknown, but probably similar to those of corticosteroids
- *Serum urate-lowering therapy*:
  - *Febuxostat*: abdominal pain, diarrhea, and musculoskeletal pain
  - *Allopurinol*: rash and reactions (including potentially serious ones); persons with the HLA-B*5801 haplotype, which is prevalent in Asian persons (including those of Han Chinese and Thai descent) and in Korean persons with stage 3 or worse chronic kidney disease, may have an increased risk for serious adverse effects with allopurinol

Contraindications

Contraindications

- Corticosteroids are contraindicated in patients with systemic fungal infections or known contraindications.
- Patients in whom nonsteroidal anti-inflammatory drugs (NSAIDs) may be contraindicated include those with renal disease, heart failure, or cirrhosis.
- Colchicine is contraindicated in patients with renal or hepatic impairment who are using potent cytochrome P450 3A4 inhibitors or P-glycoprotein inhibitors.

Qualifying Statements

Qualifying Statements

- Clinical practice guidelines are "guides" only and may not apply to all patients and all clinical situations. Thus, they are not intended to override clinicians' judgment. All American College of Physicians (ACP) clinical practice guidelines are considered automatically withdrawn or invalid 5 years after publication or once an update has been issued.
- The authors of this article are responsible for its contents, including any clinical or treatment recommendations.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Qaseem A, Harris RP, Forciea MA, Clinical Guidelines Committee of the American College of Physicians. Management of acute and recurrent gout: a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2017 Jan 3;166(1):58-68. [94 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Jan 3

Guideline Developer(s)

American College of Physicians - Medical Specialty Society

Source(s) of Funding

Financial support for the development of this guideline comes exclusively from the American College of Physicians (ACP) operating budget.

Guideline Committee

Clinical Guidelines Committee of the American College of Physicians

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Dr. Barry reports grants and personal fees from the Informed Medical Decisions Foundation and Healthwise outside the submitted work. Dr. Boyd reports royalties from UpToDate outside the submitted work. Authors not named here have disclosed no conflicts of interest. Authors followed the policy regarding conflicts of interest described at www.annals.org/aim/article/745942. Disclosures can also be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M16-0570. All financial and intellectual disclosures of interest were declared, and potential conflicts were discussed and managed. Dr. Manaker was recused from voting on this guideline because of an active indirect financial conflict. Dr. McLean was recused from voting on this guideline because of an inactive direct financial conflict. A record of disclosures of interest and management of conflicts of interest is kept for each Clinical Guidelines Committee meeting and conference call and can be viewed at www.acponline.org/about-acp/who-we-are/leadership/committees-boards-councils/clinical-guidelines-committee/disclosure-of-interests-for-clinical-guidelines-committee.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Annals of Internal Medicine Web site .

Availability of Companion Documents

The following are available:

Shekelle PG, Newberry SJ, FitzGerald JD, Motala A, O'Hanlon CE, Tariq A, Okunogbe A, Han D, Shanman R. Management of gout: a systematic review in support of an American College of Physicians clinical practice guideline. Ann Intern Med. 2017 Jan 3;166(1):37-51. Available from the Annals of Internal Medicine Web site .

Shekelle PG, FitzGerald J, Newberry SJ, Motala A, O'Hanlon CE, Okunogbe A, Tariq A, Han D, Dudley W, Shanman R, Booth M. Management of gout. Comparative effectiveness review no. 176. (Prepared by the RAND Southern California Evidence-based Practice Center under Contract no. 290-2012-00006-I.) AHRQ Publication no.16-EHC017-EF. Rockville (MD): Agency for Healthcare Research and Quality; 2016 Mar. Addendum 2016 Oct. 199 p. Available from the Agency for Healthcare Research and Quality (AHRQ) Web site .

Qaseem A, Snow V, Owens DK, Shekelle P. The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010 Aug 3;153(3):194-9. Available from the Annals of Internal Medicine Web site .

Patient Resources

The following is available:

Diagnosis and management of gout: clinical practice guidelines from the American College of Physicians. Summaries for patients. Ann Intern Med. 2017 Jan 3;166(1):I-16. Available from the Annals of Internal Medicine Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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